CHEM 344 Summer 2015 Midterm Exam (100 pts)

Name:

TA Name:

DO NOT REMOVE ANY PAGES FROM THIS EXAM PACKET.

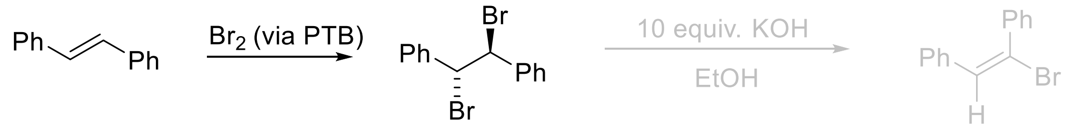
Directions for drawing molecules and electron-pushing mechanisms:

Draw all lone pairs, bonds, arrows, formal charges, and stereochemistry explicitly in all molecular structures.

Directions for analyzing graded spectra:

- Label each set of equivalent protons using the H_a, H_b, H_c etc. labeling system. Assign each **^{1}H-NMR** signal and write your assignments directly onto the spectrum. Use the empirical chemical shift parameters (Curphy-Morrison parameters) or chemical shift tables found at the end of the exam to ***assist*** your ^{1}H-NMR analysis and signal assignments.
- Assign the hybridization of the ^{13}C-atoms responsible for each **^{13}C-NMR** signal. Identify specific functional group signals; you do not need to assign individual carbon atoms to each signal.
- Assign each key **IR** absorption band >1500 cm^{-1} to a specific functional group. Draw a part structure responsible for the vibration next to each band.
- Draw fragments for all labeled peaks in the **EI-MS** directly onto the spectrum (you do not need to show the fragmentation mechanism unless directed to do so).

1) In a microwave-assisted reaction, a stilbene dibromide is reacted with potassium hydroxide in an attempt to generate a vinyl bromide by loss of HBr. The stilbene dibromide (*meso*-1,2-dibromo-1,2-diphenylethane) is generated by reaction of *trans*-stilbene with Br_2 generated by pyridinium tribromide. Read the two procedures below and answer the subsequent questions. **(39 pts total)**



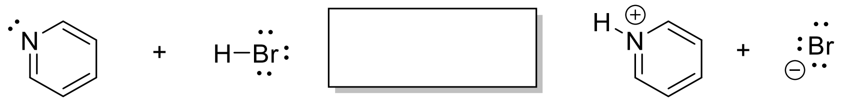
trans-stilbene (**1**) *meso*-dibromo-1,2-diphenylethane (**2**) target vinyl bromide (**3**)

Experimental Procedure

Bromination of *trans*-stilbene (1)

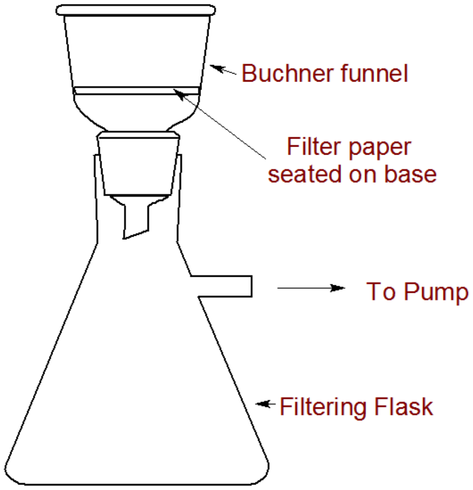
Add trans-stilbene (1.03 g) into a 25 mL flask containing a stir bar. Add acetic acid (10 mL) to the flask, and gently heat the colorless solution on a hotplate with stirring. Add solid pyridinium tribromide (PTB) (2.00 g) in portions to the stirred solution of trans-stilbene until the deep color of the reaction mixture has dissipated. Cool the reaction mixture to room temperature until a solid precipitates. Collect the solid by vacuum filtration, wash with ice-cold methanol (5 mL), and allow to air-dry for 15 min. Obtain the mass, % yield, and melting range of the dry meso-1,2-dibromo-1,2-diphenylethane (**2**).

a) In this synthetic procedure, Br_2 is generated by the thermal decomposition of pyridium tribromide (PTB). Show the pK_a values of the acids involved in this reaction to determine the favored side of the equilibrium for each acid-base reaction and draw an appropriate arrow in the box below. (The pK_a of pyridinium is 5.25. **(2 pts)**

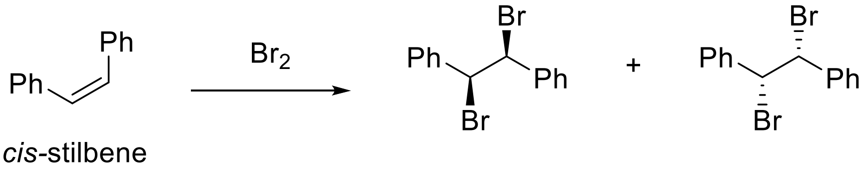


b) Ice-cold methanol is used to wash the solid product in the bromination of *trans*-stilbene. Explain why a polar protic solvent such as methanol is a reasonable choice in this case. Additionally, explain why use of hot methanol would be less effective. **(3 pts)**

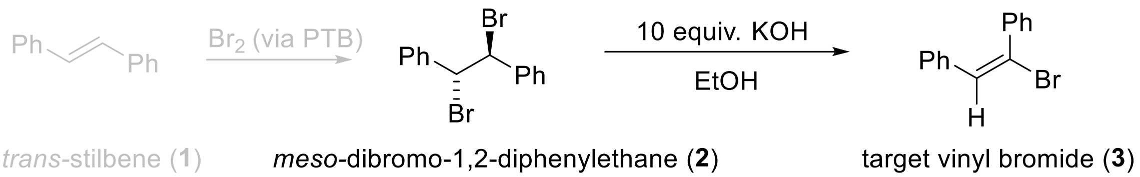
c) Vacuum filtration is a separation technique designed to purify a heterogeneous mixture of solution and solid. The vacuum filtration of the crude product mixture is shown below. Indicate where you would expect to find the majority of the *meso*-1,2-dibromo-1,2-diphenylethane (**2**), methanol, pyridinium bromide, pyridinium tribromide (**PTB**), and *trans*-stilbene (**1**). **(3 pts)**



d) The reaction of *trans*-stilbene generates a *meso* compound which can be identified by its melting range or decomposition temperature. The analogous bromination reaction of *cis*-stilbene generates two different compounds (*R,R*)-1,2-dibromo-1,2-diphenylethane and (*S,S*)-1,2-dibromo-1,2-diphenylethane. Identify the stereochemical relationship between these two compounds, and explain how would you expect their melting temperatures to compare to one another? **(3 pts)**



Reaction of 2 with KOH



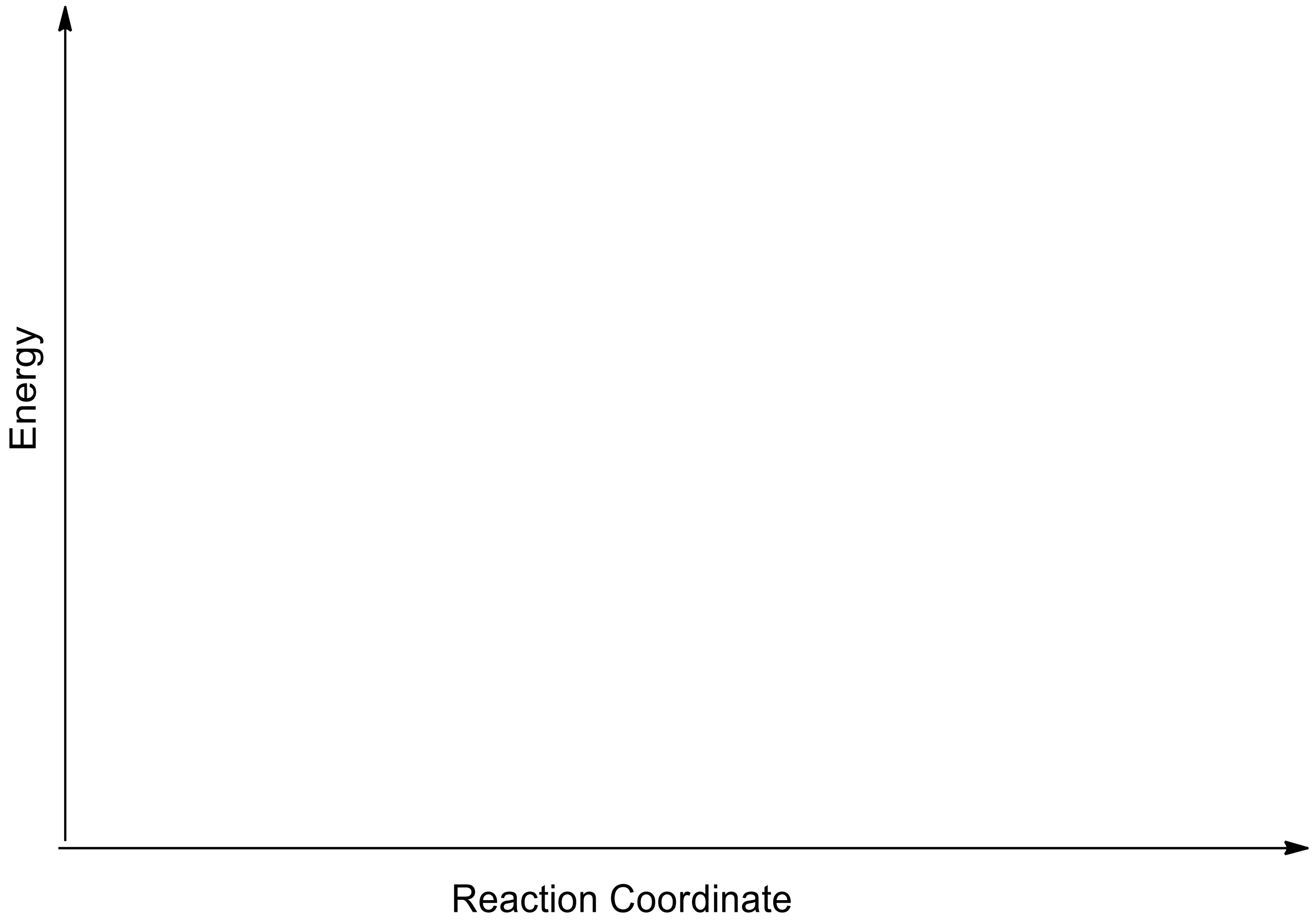
Add 20 % KOH in EtOH solution (15 mL) to a microwave sample tube and add a small stir bar. To the stirred solution in the microwave tube, add meso-1,2-dibromo-1,2-diphenylethane (1.00 g), cap the tube, and place the sample in the autosampler rack. The microwave method heats the sample to 160 °C for 5 minutes at 100 W.

Allow the sample tube to cool to room temperature. The sample tube contains a white solid and a solution. Pour the contents of the tube into ice-cold water (10 mL) in a 50 mL beaker. The initial white solid should dissolve and a slightly off-white, voluminous solid should precipitate. Isolate the newly precipitated solid by vacuum filtration, rinse with ice-cold water (5 mL), and allow the sample to air-dry for 15 min. Obtain the mass, % yield, and melting range of the dry product.

e) Potassium hydroxide, $KOH_{(s)}$, is not likely to be the active base in the reaction to produce the target product. Provide a balanced chemical reaction showing the formation of ethoxide. **(2 pts)**

f) Draw an electron-pushing mechanism for the reaction of *meso*-1,2-dibromo-1,2-diphenylethane (**2**) with a single equivalent of ethoxide. **(3 pts)**

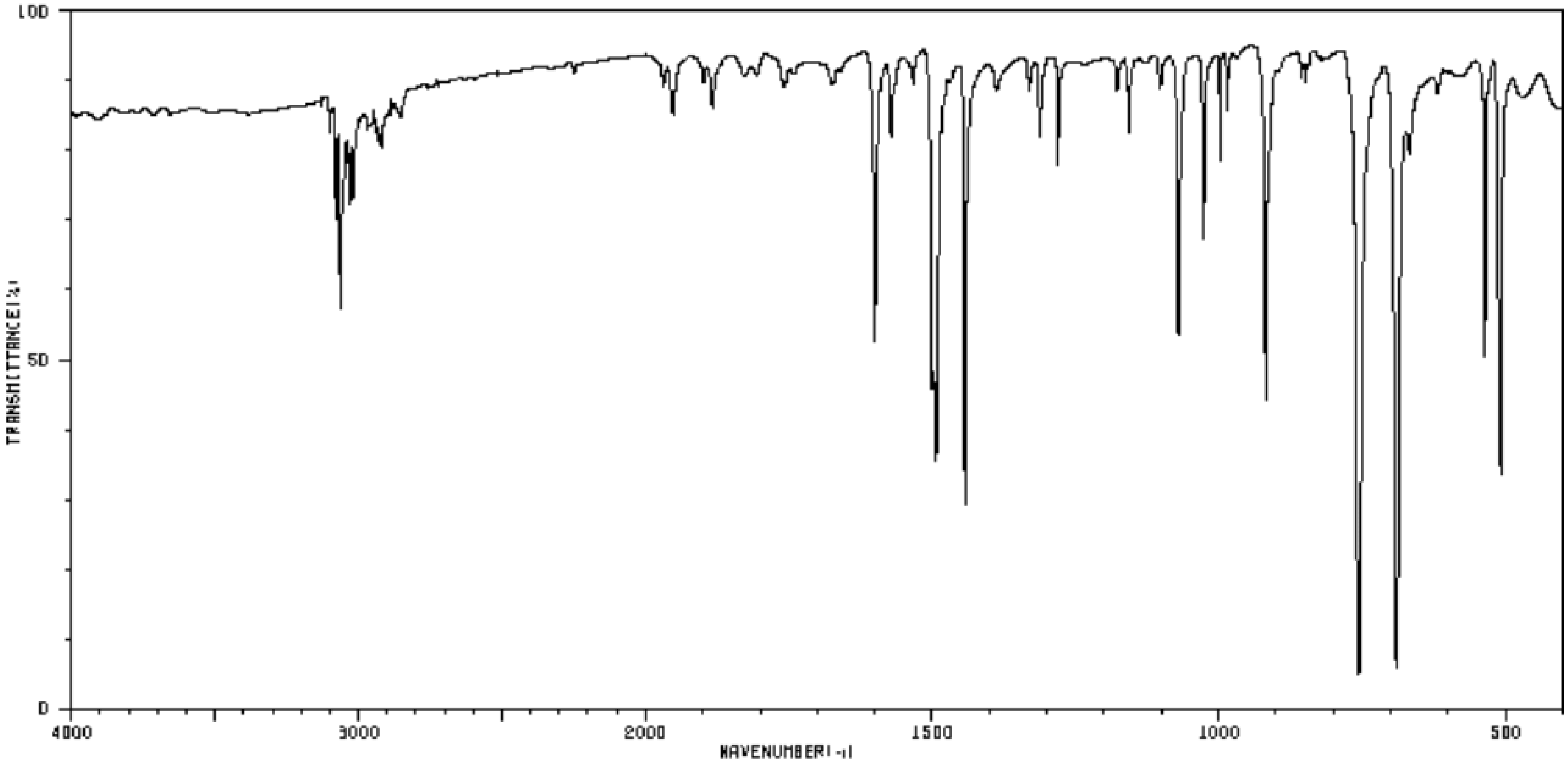
g) Draw a potential energy surface (PES) for the reaction of a single equivalent of ethoxide with *meso*-1,2-dibromo-1,2-diphenylethane (**2**) that is consistent with the electron-pushing mechanism in part f). Draw each species [reactant(s), intermediate(s), transition state(s) and/or product(s)] directly on the PES using the axes provided below. **(6 pts)** Clearly identify the Gibbs free energy difference on the PES that controls the rate of reaction. Explain briefly whether the reaction is under thermodynamic or kinetic control. **(2 pts)**



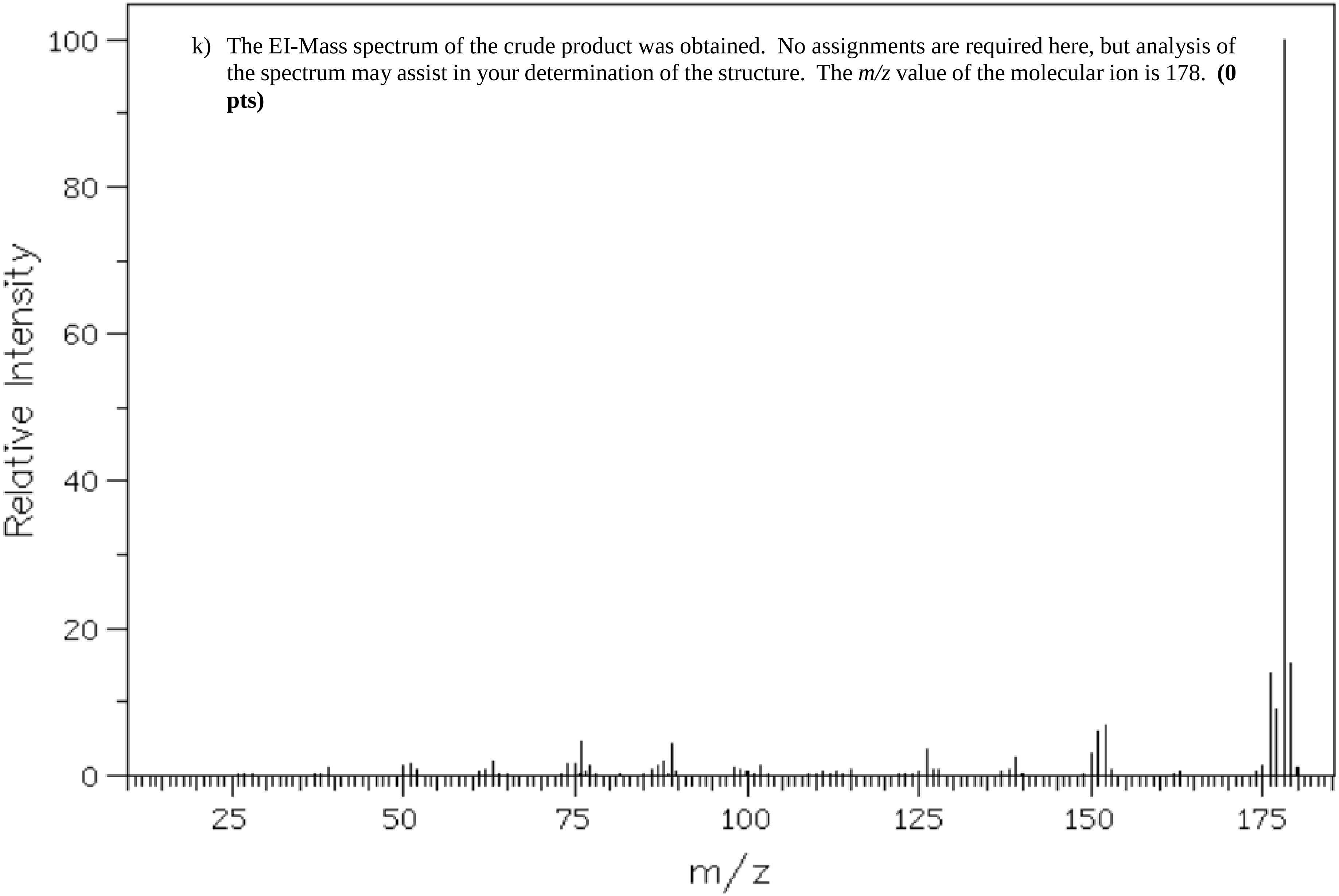
h) The compound *meso*-1,2-dibromo-1,2-diphenylethane (**2**) was reacted with a large excess of base in the microwave tube. A white solid precipitated from solution following cooling of the microwave sample tube. After adding the crude reaction mixture to ice-cold water, the original white solid dissolved and the organic product of the reaction precipitated. What was the original, water-soluble white solid? **(2 pts)**

i) The major organic product of the reaction was collected by vacuum filtration. Use the following EI-MS, IR, ^{13}C-NMR and ^{1}H-NMR spectra to determine the structure of the organic product obtained from reaction of *meso*-1,2-dibromo-1,2-diphenylethane (**2**) with a large excess of base. Analyze each graded spectrum fully as per the directions on page 1. Draw the structure of the major product in the box below. **(3 pts)**

j) The IR spectrum of the crude product was obtained. Assign each key IR absorption band >1500 cm^{-1} to a specific functional group. Draw a part structure responsible for the vibration next to each band. **(2 pts)**

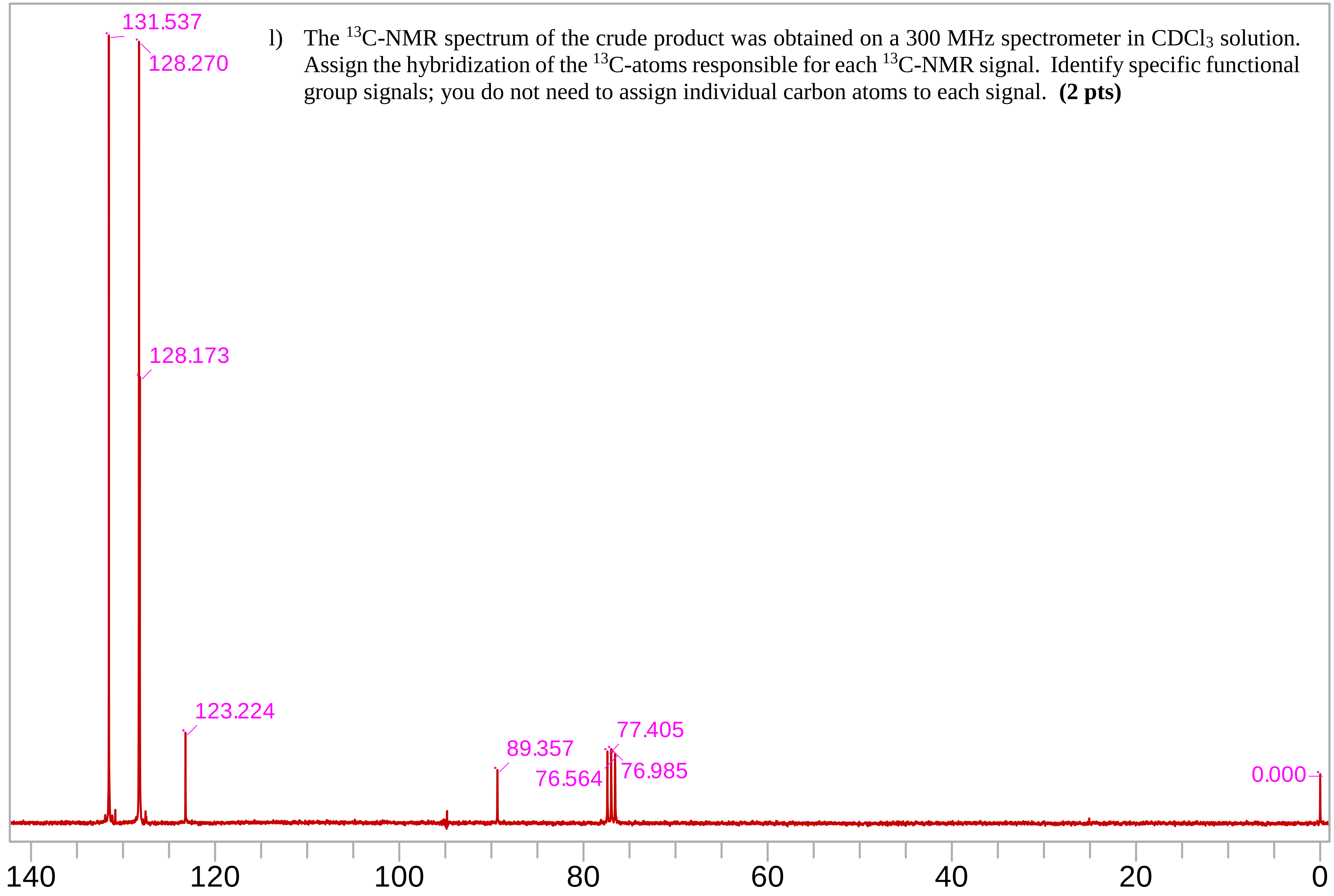


k) The EI-Mass spectrum of the crude product was obtained. No assignments are required here, but analysis of the spectrum may assist in your determination of the structure. The *m/z* value of the molecular ion is 178. **(0 pts)**



75 MHz ^{13}C NMR

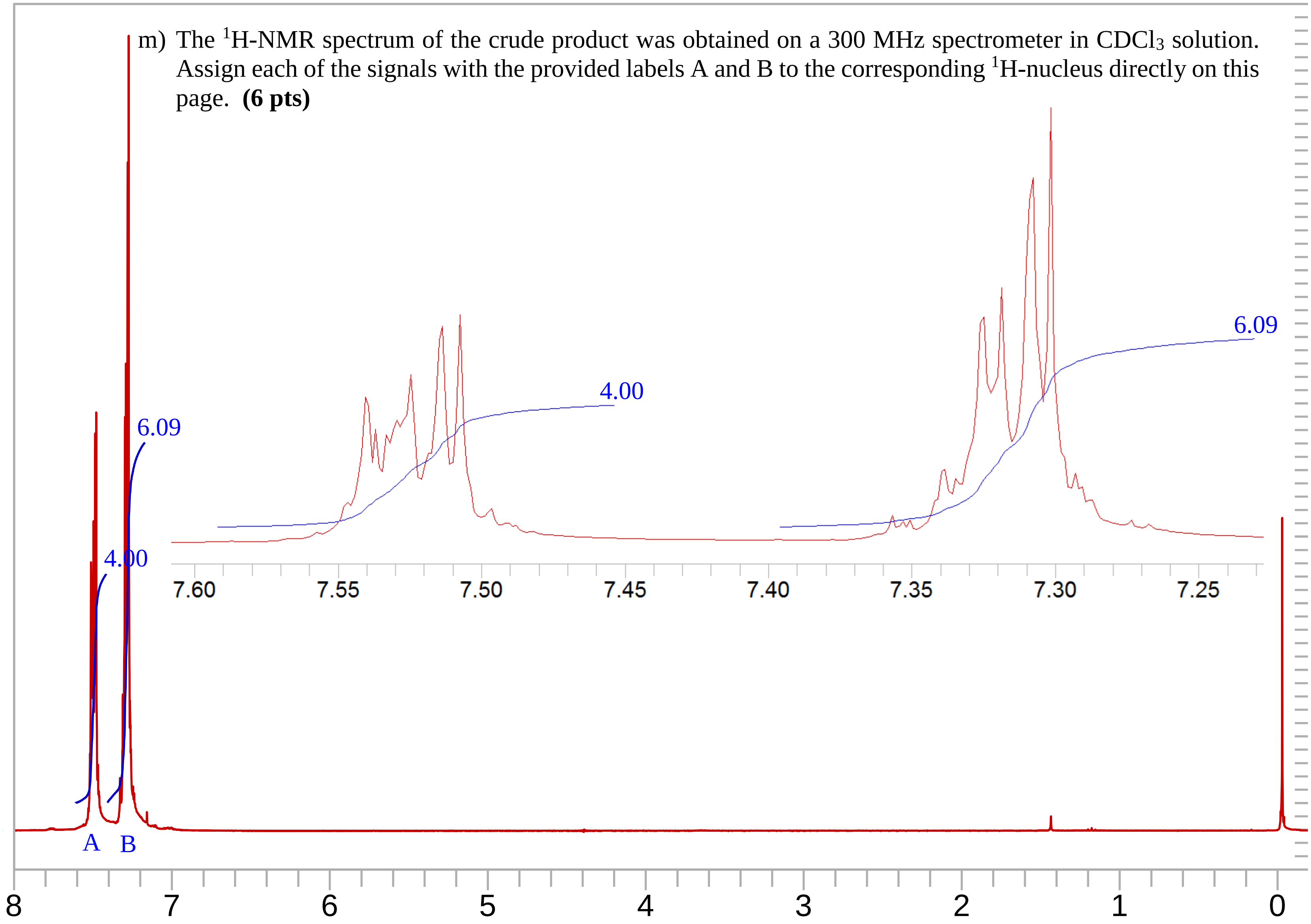
In $CDCl_3$



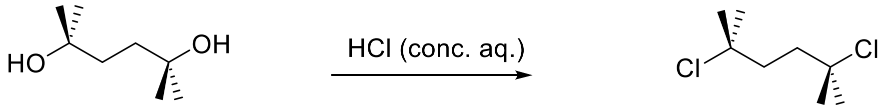
l) The ^{13}C-NMR spectrum of the crude product was obtained on a 300 MHz spectrometer in $CDCl_3$ solution. Assign the hybridization of the ^{13}C-atoms responsible for each ^{13}C-NMR signal. Identify specific functional group signals; you do not need to assign individual carbon atoms to each signal. **(2 pts)**

300 MHz ^{1}H NMR
In $CDCl_3$

m) The ^{1}H-NMR spectrum of the crude product was obtained on a 300 MHz spectrometer in $CDCl_3$ solution. Assign each of the signals with the provided labels A and B to the corresponding ^{1}H-nucleus directly on this page. **(6 pts)**



2) The chloroalkane 2,5-dichloro-2,5-dimethylhexane can be synthesized in one step from 2,5-dimethyl-2,5-hexanediol using the procedure described below. Use the procedure and reaction below to answer the subsequent questions. **(45 pts total)**



2,5-dimethyl-2,5-hexandiol
MW = 146.23

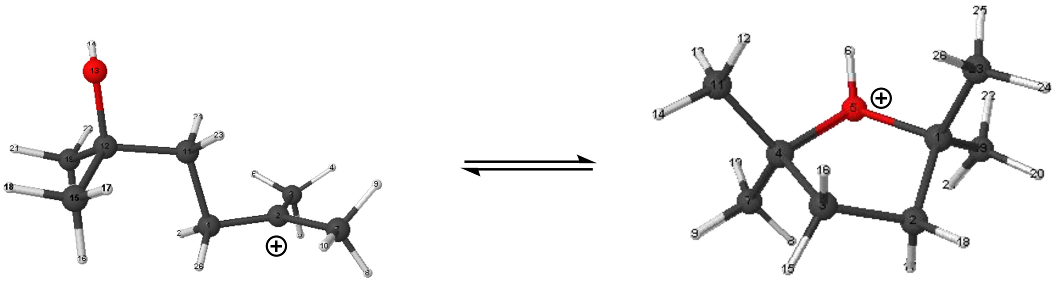
2,5-dichloro-2,5-dimethylhexane
MW = 183.12

Experimental Procedure

Add 2,5-dimethyl-2,5-hexanediol (0.25 g, 1.71 mmol) to 25 mL Erlenmeyer flask. Add conc. HCl (5 mL) to the flask and gently stir the contents for 10 minutes. After this time, isolate the solid product by vacuum filtration, wash with sat. aq. $NaHCO_3$ *solution (2 x 5 mL) followed by ice-cold water (2 x 5 mL), and allow to air-dry for 15 min. Obtain the mass, % yield, and melting range of the dried 2,5-dichloro-2,5-dimethylhexane.*

a) The reaction above works successfully with conc. HCl solution but not with NaCl(s). Explain the role(s) or purpose(s) of HCl in this chemical reaction. **(4 pts)**

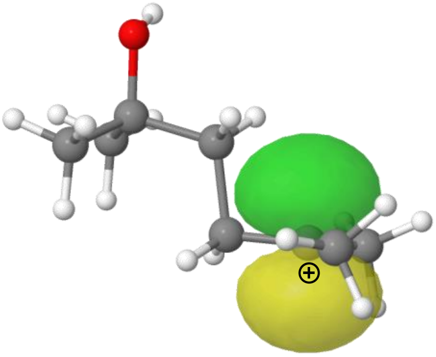
b) The reaction mechanism for the conversion of 2,5-dimethyl-2,5-hexanediol to 2,5-dichloro-2,5-dimethylhexane involves an equilibrium between the two cationic intermediates shown below. Determine the relative energies of the two intermediates in kcal/mol. 627.509 kcal/mol = 1 Hartrees/particle **(2 pts)**



-390.0305597 Hartrees/particle

-390.070255 Hartrees/particle

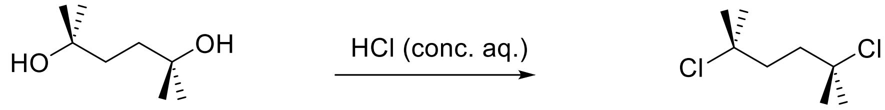
c) Determine the approximate hybridization of the carbon atom bearing the yellow/green orbital (image below is of an NBO depiction of the LUMO for the leftmost intermediate in part b). Although located on a cationic carbon atom, the formally *empty* orbital actually contains significant electron density. From where does this electron density come? **(4 pts)**



occupancy = 0.477 electrons

d) A sample of 0.26 g 2,5-dichloro-2,5-dimethylhexane was obtained from the reaction of 2,5-dimethyl-2,5-hexanediol with conc. HCl solution. Showing all work, calculate the % yield of 2,5-dichloro-2,5-dimethylhexane. **(4 pts)**

e) Using both the cationic species above in parts b) and c), draw an electron-pushing mechanism that accounts for the observed product of the reaction. **(8 pts)**



2,5-dimethyl-2,5-hexandiol

2,5-dichloro-2,5-dimethylhexane

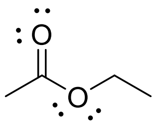
f) Explain the purpose of washing the isolated product first with sat. aq. $NaHCO_3$ followed by ice-cold water during the purification process. Show a balanced chemical reaction for the first wash. **(4 pts)**

g) The TLC plate below shows a sample of 2,5-dimethyl-2,5-hexanediol on the left and a sample of purified 2,5-dichloro-2,5-dimethylhexane on the right. (You do not need to analyze the middle spot, which was an intentional mixture of the starting material and product.) The TLC plate was run using a 20:80 mixture of ethyl acetate:hexanes as solvent and developed with PMA stain.

What can be concluded about the effectiveness of the purification in the procedure? Make specific reference to the TLC image. **(3 pts)**

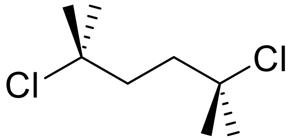
h) Calculate the R_f value of the starting material and the product of the reaction. What is the cause of the lower R_f value for the leftmost spot? **(4 pts)**

i) The TLC solvent used in this procedure is 20:80 ethyl acetate:hexane. Explain how would you expect the R_f value of 2,5-dimethyl-2,5-hexanediol to change if 80:20 ethyl acetate:hexane was used as the TLC solvent. **(3 pts)**

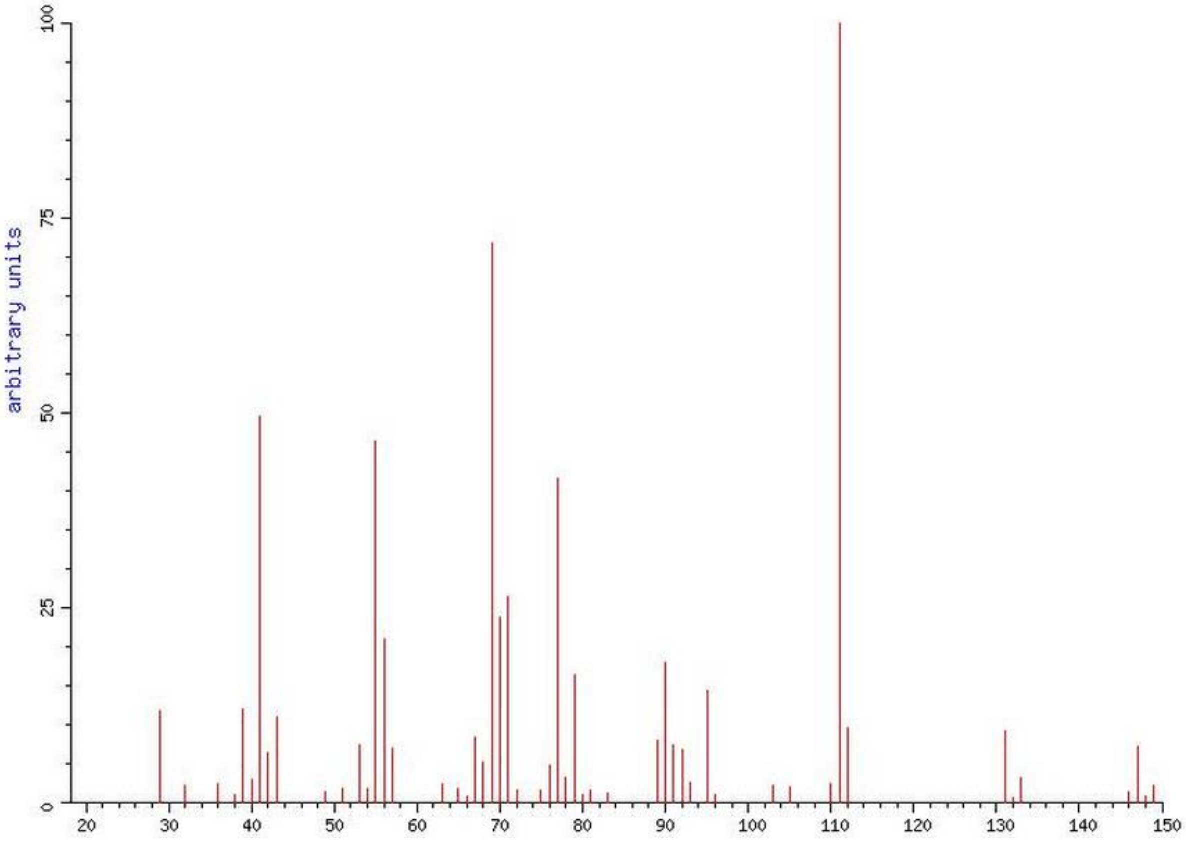


ethyl acetate

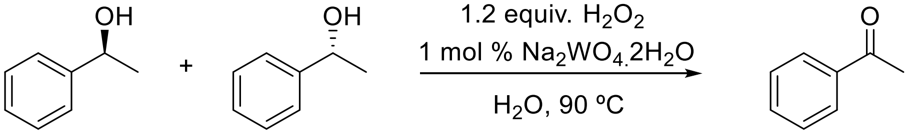
j) Use empirical (Curphy-Morrison) parameters to predict the ^{1}H-NMR chemical shifts of the ^{1}H-nuclei in 2,5-dichloro-2,5-dimethylhexane. Additionally, provide the expected coupling value (*J*, Hz) and coupling pattern for each signal in the ^{1}H-NMR spectrum. **(6 pts)**



k) The EI-Mass spectrum of 2,5-dichloro-2,5-dimethylhexane is provided below. Provide a plausible explanation for the relative intensity ratios observed between the peaks at *m/z* =131 and 133. **(3 pts)**



3) Using an equivalent of hydrogen peroxide and a catalytic amount of a tungsten-containing oxidizing agent (sodium tungstate dihydrate, $Na_2WO_4.2H_2O$), 1-phenylethanol can be oxidized to acetophenone in high yield via the procedure described below. **(16 pts total)**



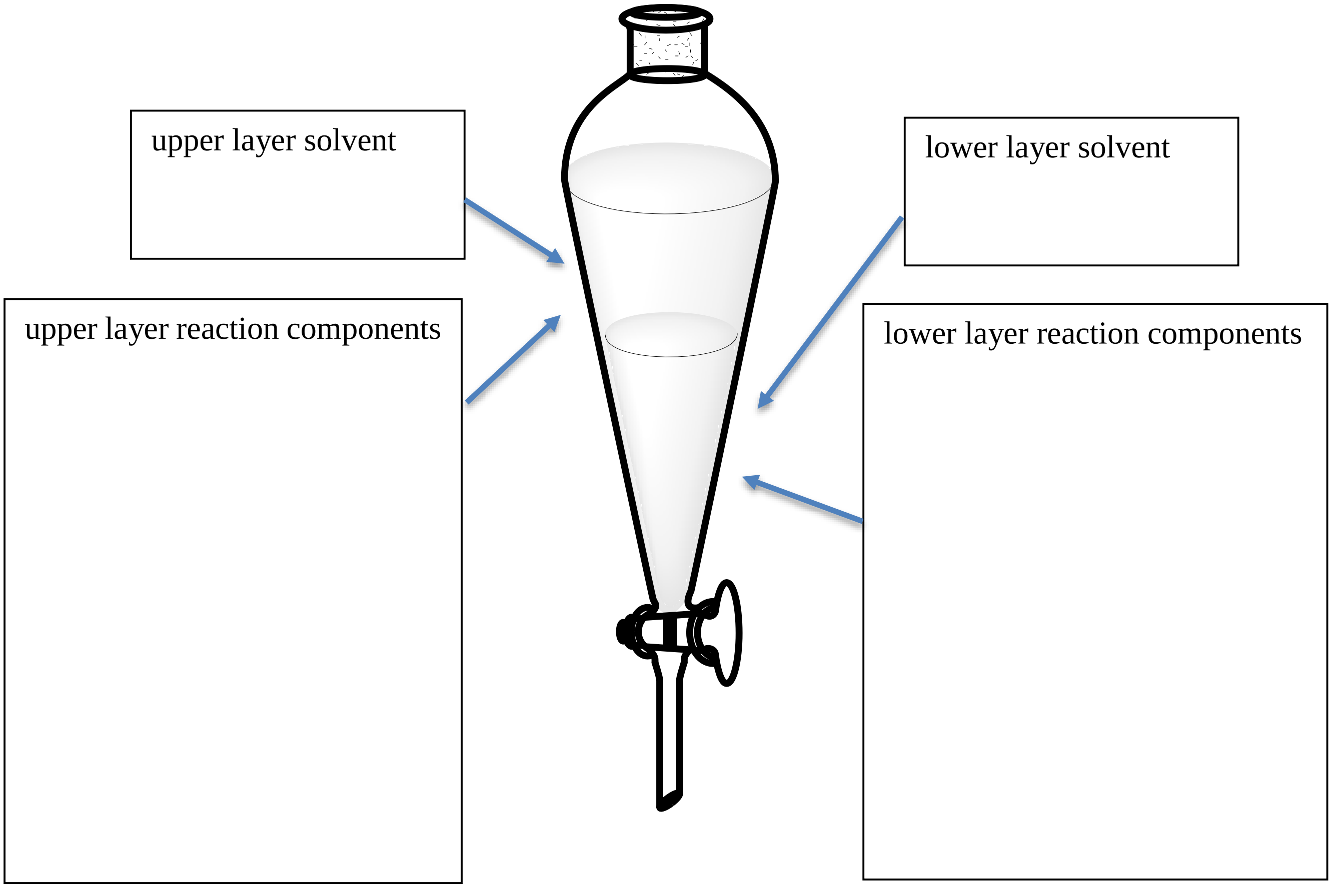
Experimental Procedure

Add $Na_2WO_4.2H_2O$ (0.042 mmol) and H_2O_2 (5.0 mmol of 30 wt % aqueous solution) to a 25 mL round bottom flask and stir the mixture rapidly at room temperature for 5 min. Add 1-phenylethanol (4.2 mmol) to the flask and attach a water-jacketed reflux condenser. Heat the flask at 80 – 90 ºC in a sand-bath for 60 min.

After this time, cool the flask in an ice-water bath and transfer the contents of the flask to a 25 mL separatory funnel. Rinse the reaction flask with H_2O (5 mL) and diethyl ether (10 mL) and add the washings to the separatory funnel. Shake the funnel and allow the layers to separate. Wash the organic layer with saturated aqueous $NaHSO_3$ solution (2 mL) and allow the layers to separate. Pass the organic layer through a Pasteur pipette containing anhydrous Na_2SO_4. Collect the organic layer in a pre-weighed flask and evaporate the diethyl ether from the solution using a gentle stream of air or nitrogen. Obtain the mass and % yield of acetophenone.

a) The reaction is heated to 80 – 90 ºC in a sand-bath using a reflux condenser. Explain the purpose of heating this reaction and using a reflux condenser. **(4 pts)**

b) After heating water and diethyl ether are added to perform an extraction using a separatory funnel. The two layers in the separatory funnel are shown below. Clearly label each solvent and place the starting material and product into their appropriate layers. **(4 pts)**



c) What is the purpose of washing the reaction mixture with aqueous $NaHSO_3$ solution? Provide a balanced chemical equation as part of your answer. **(4 pts)**

d) What is the purpose of passing the reaction mixture through a column of anhydrous Na_2SO_4? Explain how Na_2SO_4 accomplishes its intended purpose. **(4 pts)**

Name:

TA Name:

1)

a) ______ /2
b) ______ /3
c) ______ /3
d) ______ /3
e) ______ /2
f) ______ /3
g) ______ /8
h) ______ /2
i) ______ /3
j) ______ /2
k) ______ /0
l) ______ /2
m) ______ /6

______ /39

2)

a) ______ /4
b) ______ /2
c) ______ /4
d) ______ /4
e) ______ /8
f) ______ /4
g) ______ /3
h) ______ /4
i) ______ /3
j) ______ /6
k) ______ /3

______ /45

3)

a) ______ /4
b) ______ /4
c) ______ /4
d) ______ /4

______ /16

Total = ______ /100

Total = ______ /100 (math double-check)